# Complete Summary

## GUIDELINE TITLE

Antithrombotic therapy in atrial fibrillation. In: Sixth ACCP Consensus Conference on Antithrombotic Therapy.

## BIBLIOGRAPHIC SOURCE(S)

Albers GW, Dalen JE, Laupacis A, Manning WJ, Petersen P, Singer DE. Antithrombotic therapy in atrial fibrillation. Chest 2001 Jan;119(1 Suppl):194S-206S. [103 references]

## COMPLETE SUMMARY CONTENT



## SCOPE

### DISEASE/CONDITION(S)

Ischemic stroke

### GUIDELINE CATEGORY

Prevention

### CLINICAL SPECIALTY

Cardiology
Emergency Medicine
Family Practice
Internal Medicine

### INTENDED USERS

Physicians

## GUIDELINE OBJECTIVE(S)

- To present evidence-based recommendations for antithrombotic therapy in patients with atrial fibrillation for the purpose of preventing strokes

## TARGET POPULATION

Patients with atrial fibrillation.

These guidelines are not intended for use in the following patients:

- Patients with atrial fibrillation associated with rheumatic mitral valve disease;
- Patients with atrial fibrillation associated with prosthetic heart valves.

Note: For information regarding rheumatic mitral valve disease and prosthetic heart valves, see the National Guideline Clearinghouse Guideline Summary titled "Valvular Heart Disease and Prosthetic Heart Valves."

## INTERVENTIONS AND PRACTICES CONSIDERED

Prevention of Strokes:

1. Adjusted dose warfarin therapy
2. Aspirin therapy

Note: Aspirin plus low-fixed-dose warfarin therapy is considered but not recommended.

## MAJOR OUTCOMES CONSIDERED

- Efficacy and safety of antithrombotic therapy in preventing strokes in patients with atrial fibrillation, as evidenced by rates of ischemic stroke, vascular death, and major bleeds
- Relative risk reduction for strokes

# METHODOLOGY

## METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Searches of Electronic Databases

## DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The participants reviewed information from an exhaustive review of the literature.

## NUMBER OF SOURCE DOCUMENTS

Not stated

## METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

## RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

The rating scheme framework captures the trade-off between benefits and risks (1 or 2) (see "Rating Scheme for the Strength of the Recommendations") and the methodologic quality of the underlying evidence (A, B, C+, or C).

Grades of evidence for antithrombotic agents:

1A
Methodological strength of supporting evidence: randomized controlled trials without important limitations

1B
Methodological strength of supporting evidence: randomized controlled trials with important limitations (inconsistent results, methodologic flaws*)

1C+
Methodological strength of supporting evidence: no randomized controlled trials, but randomized controlled trial results can be unequivocally extrapolated; or, overwhelming evidence from observational studies

1C
Methodological strength of supporting evidence: observation studies

2A
Methodological strength of supporting evidence: randomized controlled trials without important limitations

2B
Methodological strength of supporting evidence: randomized controlled trials with important limitations (inconsistent results, methodologic flaws*)

2C
Methodological strength of supporting evidence: observational studies

* Such situations include randomized controlled trials with lack of blinding, and subjective outcomes, in which the risk of bias in measurement of outcomes is high; and randomized controlled trials with large loss to follow-up.

## METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review with Evidence Tables

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Consensus Development Conference)

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The strength of any recommendation depends on two factors: the trade-off between benefits and risks, and the strength of the methodology that leads to estimates of the treatment effect. The rating scheme used for this guideline captures these factors. The guideline developers grade the trade-off between benefits and risks in two categories: (1) the trade-off is clear enough that most patients, despite differences in values, would make the same choice; and (2) the trade-off is less clear, and each patient's values will likely lead to different choices.

When randomized trials provide precise estimates suggesting large treatment effects, and risks and costs of therapy are small, treatment for average patients with compatible values and preferences can be confidently recommended.

If the balance between benefits and risks is uncertain, methodologically rigorous studies providing grade A evidence and recommendations may still be weak (grade 2). Uncertainty may come from less precise estimates of benefit, harm, or costs, or from small effect sizes.

There is an independent impact of validity/consistency and the balance of positive and negative impacts of treatment on the strength of recommendations. In situations when there is doubt about the value of the trade-off, any recommendation will be weaker, moving from grade 1 to grade 2.

Grade 1 recommendations can only be made when there are precise estimates of both benefit and harm, and the balance between the two clearly favors recommending or not recommending the intervention for the average patient with compatible values and preferences. Table 2 of the original guideline document summarizes how a number of factors can reduce the strength of a recommendation, moving it from grade 1 to grade 2. Uncertainty about a recommendation to treat may be introduced if the target event that is trying to be prevented is less important (confident recommendations are more likely to be made to prevent death or stroke than asymptomatic deep venous thrombosis); if the magnitude of risk reduction in the overall group is small; if the risk is low in a particular subgroup of patients; if the estimate of the treatment effect, reflected in a wide confidence interval (CI) around the effect, is imprecise; if there is substantial potential harm associated with therapy; or if there is an expectation for a wide divergence in values even among average or typical patients. Higher costs would also lead to weaker recommendations to treat.

The more balanced the trade-off between benefits and risks, the greater the influence of individual patient values in decision making. If they understand the benefits and risks, virtually all patients will take aspirin after myocardial infarction

or will comply with prophylaxis to reduce thromboembolism after hip replacement. Thus, one way of thinking about a grade 1 recommendation is that variability in patient values or individual physician values is unlikely to influence treatment choice in average or typical patients.

When the trade-off between benefits and risks is less clear, individual patient values will influence treatment decisions even among patients with average or typical preferences.

Grade 2 recommendations are those in which variation in patient values or individual physician values will often mandate different treatment choices, even among average or typical patients.

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

The rating scheme framework captures the trade-off between benefits and risks (1 or 2) and the methodologic quality of the underlying evidence (A, B, C+, or C) (see "Rating Scheme for the Strength of the Evidence").

Grades of recommendation for antithrombotic agents:

1A
Clarity of risk/benefit: risk/benefit clear
Implications: strong recommendation; can apply to most circumstances, without reservation

1B
Clarity of risk/benefit: risk/benefit clear
Implications: strong recommendation; likely to apply to most patients

1C+
Clarity of risk/benefit: risk/benefit clear
Implications: strong recommendation; can apply to most patients in most circumstances

1C
Clarity of risk/benefit: risk/benefit clear
Implications: intermediate-strength recommendation; may change when stronger evidence available

2A
Clarity of risk/benefit: risk/benefit unclear
Implications: intermediate strength recommendation; best action may differ, depending on circumstances or patients' societal values

2B
Clarity of risk/benefit: risk/benefit unclear
Implications: weak recommendation; alternative approaches likely to be better for some patients under some circumstances

2C
Clarity of risk/benefit: risk/benefit unclear
Implications: very weak recommendation; other alternatives may be equally reasonable

### COST ANALYSIS

#### Anticoagulation for Elective Cardioversion

Data from several studies currently suggest rates of thromboembolism that are similar to those associated with standard therapy, with the advantages of an earlier recovery of atrial mechanical function, ease of anticoagulation management, elimination of the need for hospital readmission for elective cardioversion, and of cost-effectiveness if performed expeditiously and without a somewhat redundant transthoracic echocardiographic examination.

### METHOD OF GUIDELINE VALIDATION

Internal Peer Review

### DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The initial guidelines were prepared by the chapter committee (the primary authors) and then reviewed separately by the Committee Co-Chairs and methodology experts and finally by the entire group of Consensus Guideline participants.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Please note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary. The recommendations that follow are based on the previous version of the guideline.

Excerpted by the National Guideline Clearinghouse (NGC):

The grading scheme is defined at the end of the Major Recommendations

#### Efficacy of Long-term Antithrombotic Therapy in Atrial Fibrillation

##### Recommended Therapy

For patients with any high-risk factor or more than one moderate-risk factor, the guideline developers recommend warfarin (target international normalized ratio 2.5; range, 2.0 to 3.0). See the National Guideline Clearinghouse summary titled "Antithrombotic Therapy in Patients With Mechanical and Biological Prosthetic Heart Valves" for target international normalized ratios in patients with mechanical heart valves. For patients with one moderate-risk factor, the guideline developers recommend aspirin, 325 milligrams per day, or warfarin (target

international normalized ratio 2.5; range, 2.0 to 3.0). For patients with no high-risk factors and no moderate-risk factors, the guideline developers recommend aspirin, 325 milligrams per day.

## Risk Stratification

High-risk factors include prior stroke/ transient ischemic attack or systemic embolus, history of hypertension, poor left ventricular systolic function, age older than 75 years, rheumatic mitral valve disease, and prosthetic heart valve. Moderate-risk factors (factors for stroke that have been identified in atrial fibrillation patients in various studies but are not as strong or consistent as the high-risk factors listed above) include age 65 to 75 years, diabetes mellitus, and coronary artery disease with preserved left ventricular systolic function.

## High-Risk Patients

1. The guideline developers recommend the use of adjusted-dose warfarin anticoagulation (target international normalized ratio 2.5; range 2.0 to 3.0) rather than aspirin in patients with atrial fibrillation at high risk for ischemic stroke because it markedly decreases the risk of ischemic stroke in patients with atrial fibrillation (grade 1A).
2. For high-risk patients, the guideline developers recommend that clinicians offer aspirin therapy if adjusted-dose warfarin is contraindicated or declined by the patient and if there are no contraindications to aspirin (grade 1A).
3. The guideline developers recommend that clinicians do not use aspirin plus low-fixed-dose warfarin therapy (grade 1A).
4. Although to our knowledge no randomized trials of oral anticoagulation have been undertaken in atrial fibrillation patients with rheumatic mitral valve disease or prosthetic heart valves (mechanical or tissue valves), the guideline developers recommend that clinicians use oral anticoagulation in these patients (grade 1C+).

## Low-Risk Patients

The guideline developers recommend that patients with atrial fibrillation who are younger than 65 years with no clinical or echocardiographic evidence of cardiovascular disease should be treated with aspirin (grade 2C).

## Moderate-Risk Patients

1. Some atrial fibrillation patients will have a risk of stroke that is between that of the high-risk and low-risk groups mentioned. For these patients, the absolute stroke risk reduction of warfarin versus aspirin is likely to be small. The guideline developers recommend the use of either oral anticoagulation or aspirin for patients with one of these moderate risk factors (grade 1A in comparison to no treatment).
2. Patients with more than one of these moderate-risk factors are at higher risk of stroke than are those with only one risk factor, and the guideline developers recommend to treat these patients in the same manner as high-risk patients (see above; grade 2C).

The ultimate choice of therapy depends on many factors, including the clinician's assessment of the magnitude of the patient's risk (for example, whether the patient has single or multiple risk factors), the ability to provide high-quality monitoring of the intensity of oral anticoagulation, the patient's risk of bleeding with oral anticoagulation, and patient preference.

Anticoagulation for Elective Cardioversion

Atrial Fibrillation

1. The guideline developers recommend that clinicians administer oral anticoagulant therapy (target international normalized ratio 2.5; range 2.0 to 3.0) for 3 weeks before and at least 4 weeks after elective direct current cardioversion of atrial fibrillation patients (grade 1C+).
2. Alternatively, the guideline developers recommend that atrial fibrillation patients undergo anticoagulation then undergo transesophageal echocardiography, and have cardioversion performed without delay if no thrombi are seen (grade 1C). For these patients, adjusted-dose warfarin therapy should still be continued until normal sinus rhythm has been maintained for at least 4 weeks.
3. Although data are limited, the risk of embolism following cardioversion in patients who have been in atrial fibrillation for less than 48 hours appears to be low. However, the guideline developers recommend the use of anticoagulation during the pericardioversion period (grade 2C).

Atrial Flutter and Supraventricular Tachycardia

1. The guideline developers recommend that clinicians manage oral anticoagulation at the time of cardioversion in patients with atrial flutter in a manner similar to that used for atrial fibrillation (grade 2C).
2. In the absence of prior thromboembolism, the guideline developers do not recommend antithrombotic therapy for cardioversion of supraventricular tachycardia (grade 2C).

Treatment of potential precipitants of atrial fibrillation (i.e., thyrotoxicosis, pneumonia, congestive heart failure) should be completed prior to attempting elective direct current cardioversion.

The rating scheme framework captures the trade-off between benefits and risks (1 or 2) and the methodologic quality of the underlying evidence (A, B, C+, or C).

Definitions:

Grades of recommendations:

1A

Clarity of risk/benefit: risk/benefit clear
Methodological strength of supporting evidence: randomized controlled trials without important limitations

Implications: strong recommendation; can apply to most circumstances, without reservation

1B

Clarity of risk/benefit: risk/benefit clear
Methodological strength of supporting evidence: randomized controlled trials with important limitations (inconsistent results, methodologic flaws*)
Implications: strong recommendation; likely to apply to most patients

1C+

Clarity of risk/benefit: risk/benefit clear
Methodological strength of supporting evidence: no randomized controlled trials, but randomized controlled trial results can be unequivocally extrapolated; or, overwhelming evidence from observational studies
Implications: strong recommendation; can apply to most patients in most circumstances

1C

Clarity of risk/benefit: risk/benefit clear
Methodological strength of supporting evidence: observation studies
Implications: intermediate-strength recommendation; may change when stronger evidence available

2A

Clarity of risk/benefit: risk/benefit unclear
Methodological strength of supporting evidence: randomized controlled trials without important limitations
Implications: intermediate strength recommendation; best action may differ, depending on circumstances or patients' societal values

2B

Clarity of risk/benefit: risk/benefit unclear
Methodological strength of supporting evidence: randomized controlled trials with important limitations (inconsistent results, methodologic flaws*)
Implications: weak recommendation; alternative approaches likely to be better for some patients under some circumstances

2C

Clarity of risk/benefit: risk/benefit unclear
Methodological strength of supporting evidence: observational studies
Implications: very weak recommendation; other alternatives may be equally reasonable

* Such situations include randomized controlled trials with lack of blinding, and subjective outcomes, in which the risk of bias in measurement of outcomes is high; and randomized controlled trials with large loss to follow-up.

### CLINICAL ALGORITHM(S)

None provided

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified for each recommendation (refer to "Major Recommendations").

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

Appropriate antithrombotic therapy in patients with atrial fibrillation may reduce the rates, relative risk, and severity of ischemic stroke, as well as the rates and severity of adverse effects, such as major bleeding. Numerous studies have demonstrated that oral anticoagulation is very effective in decreasing the risk of stroke in patients with atrial fibrillation and that it is considerably more effective than daily aspirin. Pooling the results of several trials in an intention-to-treat analysis revealed an annual stroke rate of 4.5% for the control patients and 1.4% for the adjusted-dose warfarin patients (relative risk reduction = 68%; 95% confidence interval, 50 to 79%; number needed to treat for 1 year = 32). The percentage of strokes that were classified as moderate, severe, or fatal ranged between 43% and 64%. Anticoagulation was effective for preventing strokes of all severities; In another trial which enrolled only patients with a transient ischemic attack or stroke within the previous 3 months, the relative risk reduction was virtually identical, although the absolute risk of stroke was higher; the annual rate of stroke in control patients was 12% versus 4% in anticoagulated patients (relative risk reduction = 66%; 95% confidence interval, 43 to 80%; p <0.001; number needed to treat = 13).

The evidence supporting the superiority of aspirin to placebo is less robust than the evidence for warfarin.

Subgroups Most Likely to Benefit:

Patients with atrial fibrillation who are at high risk for stroke but who do not have a high risk of bleeding are most likely to benefit from oral anticoagulation.

### POTENTIAL HARMS

Oral anticoagulation is associated with a higher frequency of hemorrhage than aspirin. Intracranial hemorrhage is the most serious complication of anticoagulant therapy, and is frequently fatal or permanently disabling.

### Subgroups Most Likely to be Harmed:

Patients at high risk for serious bleeding, whether due to established concomitant disease or inability to control the international normalized ratio are most likely to be harmed by oral anticoagulation. Each individual patient's risk of stroke and hemorrhage must be considered when making the decision about the best antithrombotic preventive therapy.

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

#### Interpreting the Recommendations

The authors of these guidelines are offering recommendations that should not be construed as dictates by the readers, including clinicians, third-party payers, institutional review committees, and courts. In general, anything other than a 1A recommendation indicates that the chapter authors acknowledge that other interpretations of the evidence and other clinical policies may be reasonable and appropriate. Even grade 1A recommendations will not apply to all circumstances and all patients. For instance, the guideline developers have been conservative in their considerations of cost, and have seldom downgraded recommendations from 1 to 2 on the basis of expense. As a result, in jurisdictions in which resource constraints are severe, alternative allocations may serve the health of the public far more than some of the interventions that we designate grade 1A. This will likely be true for all less-industrialized countries. However, a weak recommendation (2C) that reduces resource consumption may be more strongly indicated in less-industrialized countries.

Similarly, following grade 1A recommendations will at times not serve the best interests of patients with atypical values or preferences. For instance, consider patients who find anticoagulant therapy extremely aversive, either because it interferes with their lifestyle (prevents participation in contact sports, for instance) or because of the need for monitoring. For such patients, clinicians may reasonably conclude that following some grade 1A recommendations for anticoagulation will be a mistake. The same may be true for patients with particular comorbidities (such as a recent GI bleed or a balance disorder with repeated falls) or other special circumstances (such as very advanced age).

The guideline developers trust that these observations convey their acknowledgment that no guidelines or recommendations can take into account the often compelling idiosyncrasies of individual clinical circumstances. No clinician and no one charged with evaluating the actions of a clinician should attempt to apply their recommendations in a rote or blanket fashion.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Living with Illness
Staying Healthy

### IOM DOMAIN

Effectiveness
Safety

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Albers GW, Dalen JE, Laupacis A, Manning WJ, Petersen P, Singer DE. Antithrombotic therapy in atrial fibrillation. Chest 2001 Jan;119(1 Suppl):194S-206S. [103 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2001 Jan

### GUIDELINE DEVELOPER(S)

American College of Chest Physicians - Medical Specialty Society

### SOURCE(S) OF FUNDING

Funding was supplied by DuPont Pharmaceuticals.

### GUIDELINE COMMITTEE

American College of Chest Physicians Consensus Panel on Antithrombotic Therapy

### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

## GUIDELINE STATUS

Please note: This guideline has been updated. The National Guideline Clearinghouse (NGC) is working to update this summary.

## GUIDELINE AVAILABILITY

Electronic copies of the updated guideline: Available from the Chest - The Cardiopulmonary and Critical Care Journal Web site.

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348.

## AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Sixth ACCP Consensus Conference on Antithrombotic Therapy (2001): quick reference guide for clinicians. Northbrook, IL: ACCP, 2001.

Electronic copies: Available in from the American College of Chest Physicians Web site. (Downloadable files intended for use with Palm OS compatible devices are available.)

Print copies: Available from the American College of Chest Physicians, Products and Registration Division, 3300 Dundee Road, Northbrook IL 60062-2348, or by calling 1 (800) 343-2227.

## PATIENT RESOURCES

None available

## NGC STATUS

This summary was completed by ECRI on July 30, 2001. The information was verified by the guideline developer as of October 31, 2001.

## COPYRIGHT STATEMENT



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